Percuta*NEO*us Coronary Intervention Followed by *M*onotherapy *IN*stead of *D*ual Antiplatelet Therapy in the *SET*ting of Acute Coronary Syndromes

The NEO-MINDSET trial

Antonione Lamartini
R2 Hemodinâmica

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BACKGROUND

12-month dual antiplatelet therapy (DAPT) with aspirin + P2Y12 inhibitor is standard for patients with acute coronary syndromes (ACS) treated with percutaneous coronary intervention (PCI).

However, DAPT is associated with increased risk of **bleeding**.

Recent evidence supports shorter DAPT strategies, with **withdrawal of aspirin after 1-3 months** followed by monotherapy with P2Y12 inhibitor.

Still, the **early post-PCI period** carries substantial risk of thrombotic and bleeding events.

IT IS UNCLEAR WHETHER AN EARLY ASPIRIN-FREE APPROACH IS EFFECTIVE AND SAFE

Byrne et al. Eur Heart J 2023; 44: 3720–3826
Davide Capodanno et al. Circulation 2023;147:1933-1944

OBJECTIVES

NEO-MINDSET, a large-scale, multicenter, randomized trial, including ACS patients treated with PCI to determine whether:

Early aspirin-free monotherapy with potent P2Y12i *versus* DAPT would be:

PRIMARY ISCHEMIC OUTCOME
NONINFERIORITY

PRIMARY BLEEDING OUTCOME
SUPERIORITY

STUDY ORGANIZATION

Steering Committee

Pedro A. Lemos (Chair)
Marcelo Franken (Co-Chair)
Patricia O. Guimarães
Andrei C. Sposito
Dominick J. Angiolillo
Fernando Bacal
José Carlos Nicolau
Marco Valgimigli
Otavio Berwanger
Patrick W. J. C. Serruys
Renato D. Lopes
Yoshinobu Onuma

Trial Leadership

Pedro A. Lemos (Chair)
Marcelo Franken (Co-Chair)
Patricia O. Guimarães, Project Coord.
Caio A. M. Tavares, trialist
Frederico Monfardini, Statistician
Silvia R. L. Assis, Statistician

Data Safety Monitoring Board (DSMB)

Christopher B. Granger (Chair)
Roberto R. Giraldez
Tiago Mendonça (Statistician)

Funding

Brazilian Ministry of Health
PRODADI-SUS

Coordinating Center

ARO Hospital Israelita Albert Einstein

Patrícia O. Guimarães
Caio A. M. Tavares
Ronaldo V. P. Soares
Diogo D. F. Moia
Camila S. N. Alburquerque
Luciana Pereira Almeida de Piano
Lailah C. C. Abrao
Bruna dos Santos Sampaio
Rosana C. Rocha
Gabriela Souza Murizine
Roberta G. R. A. P. Momesso
Elaine de Jesus Santos
Cintia Selles Santos
Silvia R. L. Assis
Frederico Monfardini
Graziele Pereira Lunas
Sanarelly Adonias Borges de Queiroz
Fabiana Teixeira Fabrete
Larissa Emidio de Franca Silva
Jaqueline Amalia de Paulo
Bruna Ladeira Moreno

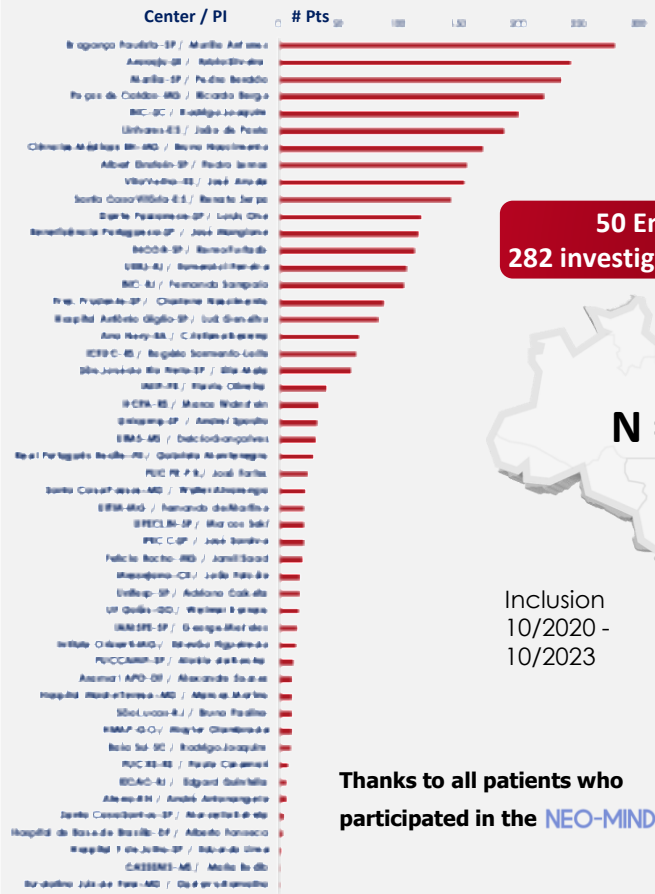
Data Analysis

ARO Hospital Israelita Albert Einstein

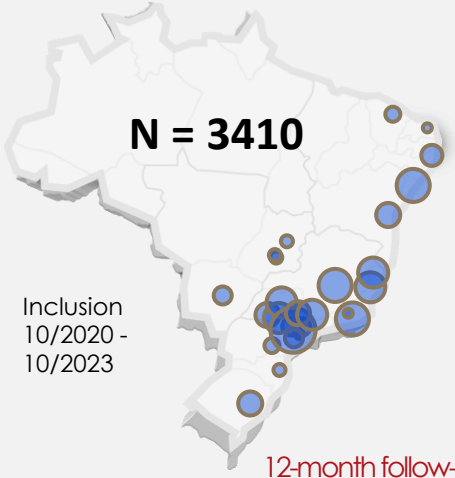
Frederico Monfardini
Silvia R. L. Assis
Gustavo P. Santos

Clinical Events Classification (CEC) Committee

Hélio Penna Guimarães (Chair)
Antonio Aurélio Fagundes Júnior
Adriano Truffa
Izabela Chaves Pedro



50 Enrolling Centers
282 investigators and study coord.



Inclusion
10/2020 -
10/2023

12-month follow-up
(99.2%)

Thanks to all patients who participated in the NEO-MINDSET

EINSTEIN Hospital Israelita Cardiologia

STUDY POPULATION

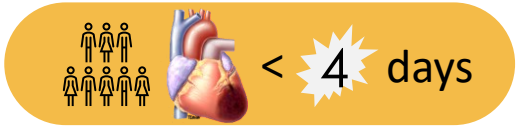
KEY INCLUSION CRITERIA

- Admitted with acute coronary syndrome (STEMI, NSTEMI, UA)
- Successful PCI of all target lesions < 4 days of admission

KEY EXCLUSION CRITERIA

- Prior ischemic stroke < 30 days
- Major active/recent bleeding, or need for oral anticoagulation, or prior intracranial bleeding, or fibrinolytics < 24 h., or bleeding diathesis.

STUDY DESIGN



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* ***Prasugrel*** *or* ***ticagrelor*** *were chosen at investigator's discretion before randomization*

MONOTHERAPY
Potent P2Y12 inhibitor*

DAPT
ASA + Potent P2Y12 inhibitor*

Unblinded DSMB review
400, 1/3, ½, 3/5, and all patients with 30-day fup

12 months

PRIMARY ISCHEMIC OUTCOME (Noninferiority)
All-cause death, MI, stroke, or urgent target vessel revascularization

Hierarchical

PRIMARY BLEEDING OUTCOME (Superiority)
Major or clinically relevant nonmajor bleeding (BARC 2, 3, or 5)

BLEEDING ACADEMIC RESEARCH CONSORTIUM SCALE [BARC]

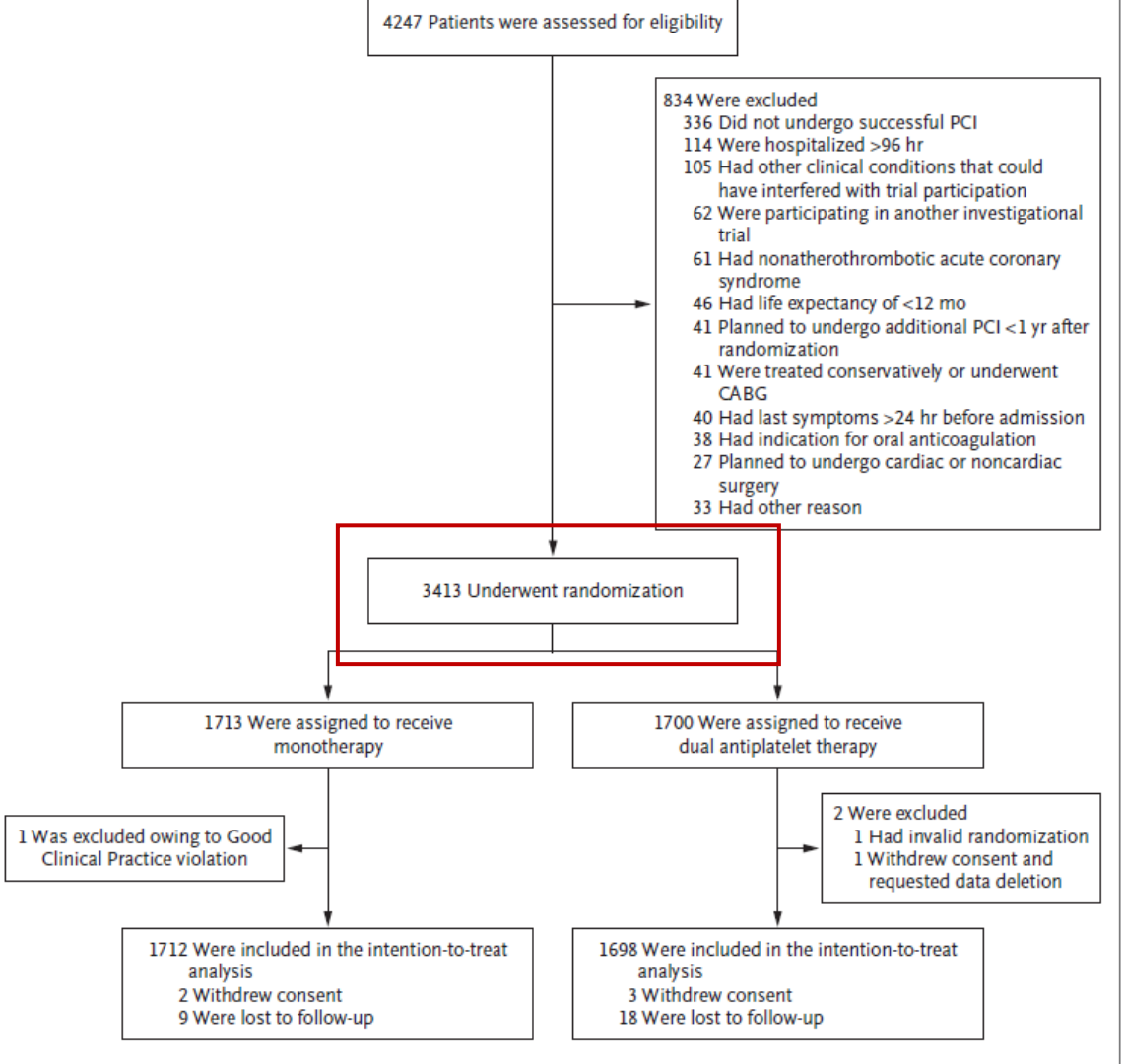
[A standardized scale to define the bleeding end point in clinic trials]

TYPE 1	Any bleeding that is not actionable	Patient does not seek unplanned medical attention
TYPE 2	Any clinically overt and actionable sign of bleeding	Requires treatment but does not fit categories below
TYPE 3	TYPE 3A	• Any transfusion, • 3-5 g/dL hemoglobin (Hb) drop
	TYPE 3B	• >5 g/dl Hb drop • Requires surgery • Requires vasopressor
	TYPE 3C	• intracerebral hemorrhage (ICH) • Intraocular bleed
TYPE 4	Bleeding related to coronary artery bypass graft (CABG) -OR-	• >5 units blood transfused in 48 h • >2L chest tube output in 24 h
TYPE 5	Likely fatal bleeding not confirmed by autopsy (5a)	Definite fatal bleeding confirmed by imaging or autopsy (5b)

Graphic by Kate Wilson @KateAlysWilson

Criteria	
ARC-HBR score=1 (n=1,910)	
Major criteria	OAC or NOAC at discharge (n=284)
	CKD (major) (n=13)
	Anaemia (major) (n=151)
	Spontaneous non-ICH bleeding (n=52)
	Thrombocytes <100×10^9/l (n=16)
	Active malignancy within past 12 months (n=40)
	ICH or stroke (n=243)
Combination of minor criteria	Age ≥75 years+CKD (minor) (n=750)
	Age ≥75 years+anaemia (minor) (n=213)
	Age ≥75 years+NSAIDS at discharge (n=15)
	CKD (minor)+anaemia (minor) (n=106)
	CKD (minor)+NSAIDS at discharge (n=6)
	Anaemia (minor)+NSAIDS at discharge (n=21)
ARC-HBR score=0.5 (n=1,982)	
Minor criteria	Age ≥75 years (n=843)
	CKD (minor) (n=314)
	Anaemia (minor) (n=739)
	NSAIDS at discharge (n=86)

STUD


4247 Patients were assessed for eligibility
834 Were excluded
336 Did not undergo successful PCI
114 Were hospitalized >96 hr
105 Had other clinical conditions that could have interfered with trial participation
62 Were participating in another investigational trial
61 Had nonatherothrombotic acute coronary syndrome
46 Had life expectancy of <12 mo
41 Planned to undergo additional PCI <1 yr after randomization
41 Were treated conservatively or underwent CABG
40 Had last symptoms >24 hr before admission
38 Had indication for oral anticoagulation
27 Planned to undergo cardiac or noncardiac surgery
33 Had other reason
3413 Underwent randomization
1713 Were assigned to receive monotherapy
1700 Were assigned to receive dual antiplatelet therapy
1 Was excluded owing to Good Clinical Practice violation
2 Were excluded
1 Had invalid randomization
1 Withdrew consent and requested data deletion
1712 Were included in the intention-to-treat analysis
2 Withdrew consent
9 Were lost to follow-up
1698 Were included in the intention-to-treat analysis
3 Withdrew consent
18 Were lost to follow-up

BASELINE & PROCEDURAL CHARACTERISTICS

	Monotherapy (n=1712)	DAPT (n=1698)
Age, y	59.5 (±10.9)	59.8 (±10.7)
Female sex	502 (29.3)	497 (29.3)
Diabetes	459 (26.8)	477 (28.1)
Qualifying index event		
STEMI	1058 (61.8)	1061 (62.5)
NSTEMI	527 (30.8)	512 (30.2)
Unstable Angina	127 (7.4)	125 (7.4)
ARC High bleeding risk	339 (19.8)	335 (19.7)
Multivessel coronary artery disease	777 (45.4)	719 (42.3)
Radial access	1465 (85.6)	1445 (85.2)
Treated vessel LAD	1010 (59.2)	999 (59.1)
At least one bifurcation lesion	219 (12.8)	184 (10.8)
Number of implanted stents	1.6 (1.0)	1.6 (1.0)
Days from admission to first PCI	1.0 (1.3)	0.9 (1.0)
Days from admission to randomization	2.3 (1.3)	2.3 (1.0)

Numbers are mean (±SD) or count (%)

ANTIPLATELET TREATMENT

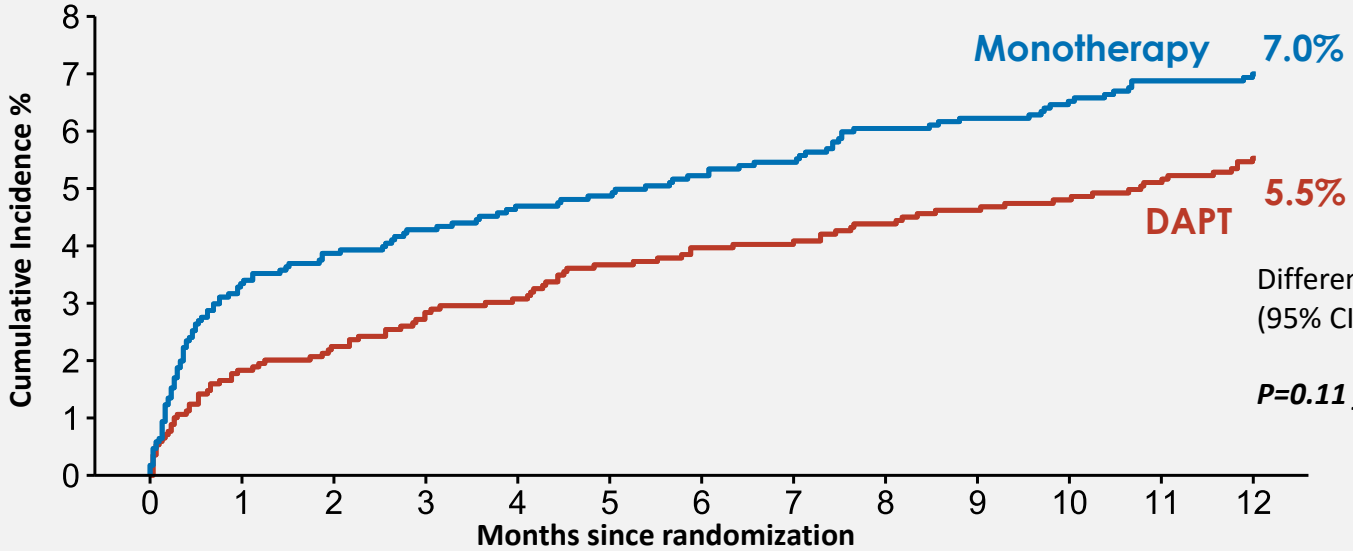
	Monotherapy (n=1712)	DAPT (n=1698)
Antiplatelet therapy before randomization		
Aspirin	1641 (95.9)	1656 (97.6)
Clopidogrel	1442 (84.3)	1439 (84.8)
Ticagrelor	136 (8.0)	129 (7.6)
Prasugrel	99 (5.8)	98 (5.8)
P2Y12 inhibitor post-randomization		
Prasugrel	1192 (69.6)	1172 (69.0)
Ticagrelor	480 (28.0)	501 (29.5)
Other	40 (2.3)	25 (1.5)

Numbers are count (%)

RESULTADOS

ISCHEMIC PRIMARY OUTCOME

All-cause death, MI, stroke, or urgent target vessel revascularization



Difference, 1.47 percentage points
(95% CI -0.16 to 3.10)

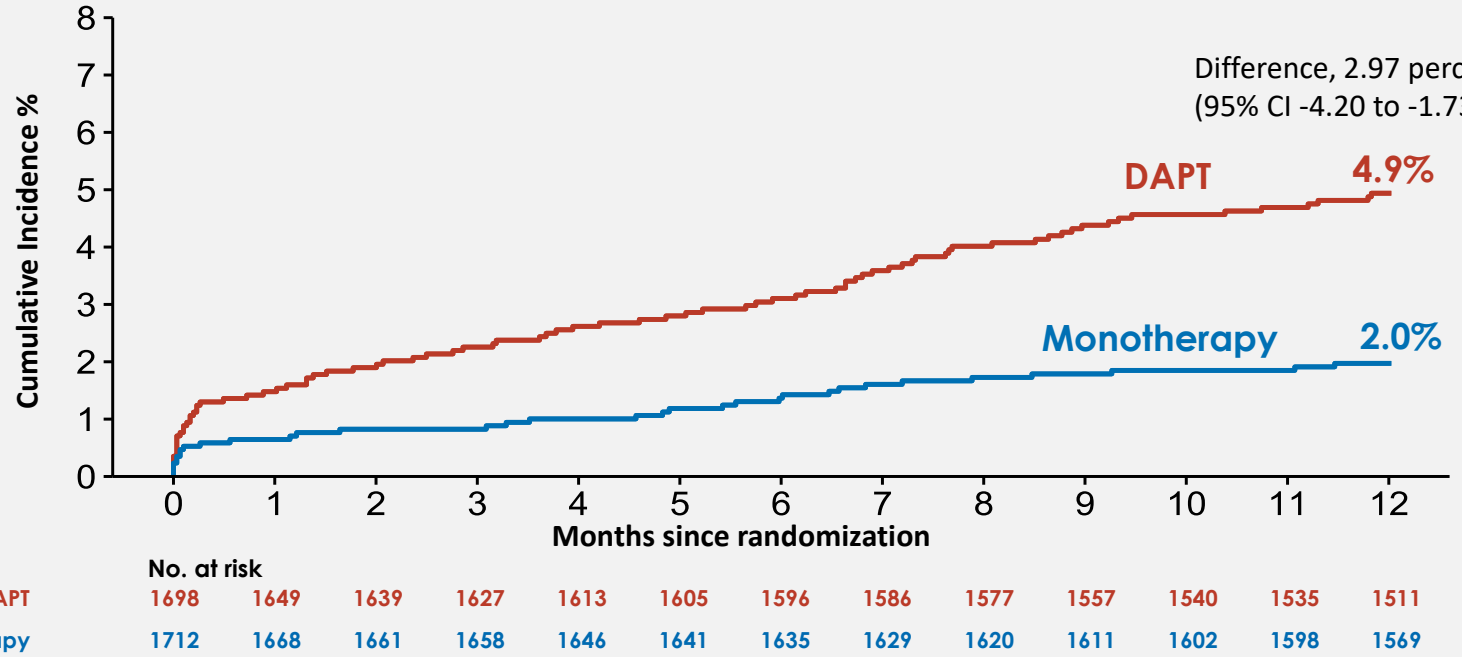
P=0.11 for noninferiority

No. at risk

DAPT	1698	1659	1652	1640	1631	1621	1616	1613	1608	1590	1577	1571	1546
Monotherapy	1712	1647	1637	1630	1620	1617	1610	1605	1595	1588	1577	1569	1543

BLEEDING PRIMARY OUTCOME

Major or Clinically Relevant Bleeding



12-MONTH SECONDARY OUTCOMES

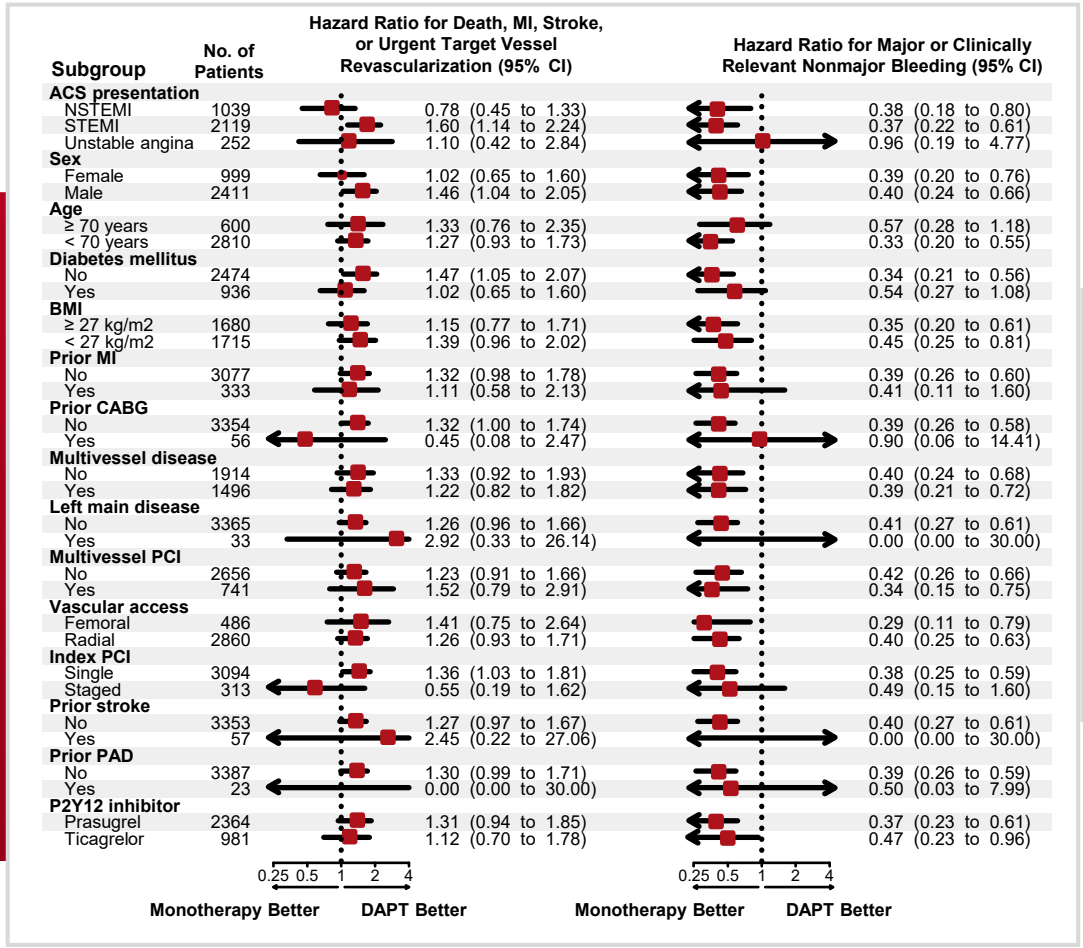
	Monotherapy (n=1712)	DAPT (n=1698)	Hazard Ratio (95% CI)
All-cause death	62 (3.6)	50 (3.0)	1.24 (0.85 to 1.79)
Cardiovascular death	42 (2.5)	34 (2.0)	1.23 (0.78 to 1.93)
Stroke	20 (1.2)	15 (0.9)	1.33 (0.68 to 2.60)
Myocardial infarction	45 (2.7)	31 (1.9)	1.45 (0.92 to 2.30)
Definite or probable stent thrombosis	12 (0.7)	4 (0.2)	2.99 (0.97 to 9.28)
Urgent target-vessel revascularization	22 (1.3)	12 (0.7)	1.83 (0.90 to 3.69)
BARC Bleeding			
Type 1 to 5	75 (4.5)	150 (9.0)	0.49 (0.37 to 0.64)
Type 1	45 (2.7)	76 (4.6)	0.58 (0.40 to 0.84)
Type 2	21 (1.3)	50 (3.0)	0.41 (0.25 to 0.69)
Type 3	11 (0.7)	33 (2.0)	0.33 (0.17 to 0.65)
Type 5	1 (0.1)	2 (0.1)	0.50 (0.05 to 5.48)
Net adverse clinical events*	145 (8.5)	166 (9.9)	0.86 (0.69 to 1.08)

*All-cause death, MI, stroke, urgent TVR, BARC 2, 3 or 5

¶ Net adverse clinical events were a composite of death from any cause, myocardial infarction, stroke, urgent target-vessel revascularization,
or a BARC type 2, 3, or 5 bleeding event.

Numbers are count (% KM estimates)

SUBGROUP ANALYSIS



All p-values for interaction terms were non-significant

CONCLUSÃO

- **Isquêmicos (morte/IAM/AVC/revasc urgente)**
  - Monoterapia: 7,0%
  - DAPT: 5,5%
  - HR 1,28 (IC95% 0,98–1,68) → **não atingiu não-inferioridade** (p=0,11).
  - **MAIS TROMBOSE DE STENT NA MONOTERAPIA: 12 CASOS VS 4**

- **Sangramento (BARC 2–5)**
  - Monoterapia: 2,0%
  - DAPT: 4,9%
  - HR 0,40 (IC95% 0,26–0,59) → redução absoluta de 3%.

CONCLUSÃO

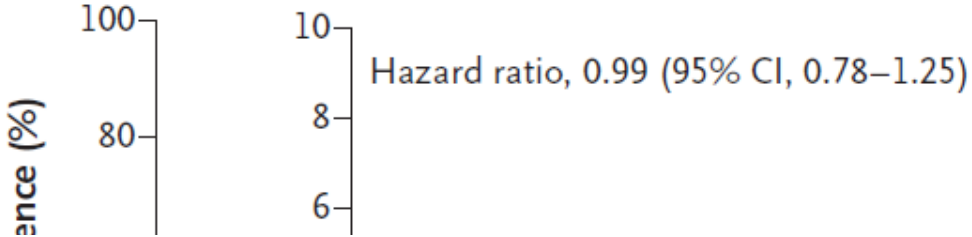
- **A retirada imediata da aspirina aumentou discretamente eventos isquêmicos**, especialmente nas primeiras semanas pós-PCI (pico de trombose subaguda de stent).

- **Sangramento reduziu pela metade**, mas não foi suficiente para compensar o aumento de isquemia.

- Estratégia parece **não segura no cenário de SCA**, ao menos com retirada tão precoce (≤4 dias).

- Confirma o conceito de que o início pós-SCA é um período **altamente protrombótico**, onde a sinergia AAS + P2Y12 ainda é crítica.

ENSAIOS CLÍNICOS



CONCLUSIONS

Among high-risk patients who underwent PCI and completed 3 months of dual antiplatelet therapy, ticagrelor monotherapy was associated with a lower incidence of clinically relevant bleeding than ticagrelor plus aspirin, with no higher risk of death, myocardial infarction, or stroke. (Funded by AstraZeneca; TWILIGHT ClinicalTrials.gov number, NCT02270242.)

	0	3	6	9	12
	Months since Randomization				
No. at Risk					
Ticagrelor plus aspirin	3515	3466	3415	3361	3320
Ticagrelor plus placebo	3524	3457	3412	3365	3330

Figure 3. Kaplan–Meier Estimates of the Incidence of Death from Any Cause, Nonfatal Myocardial Infarction, or Nonfatal Stroke 1 Year after Randomization

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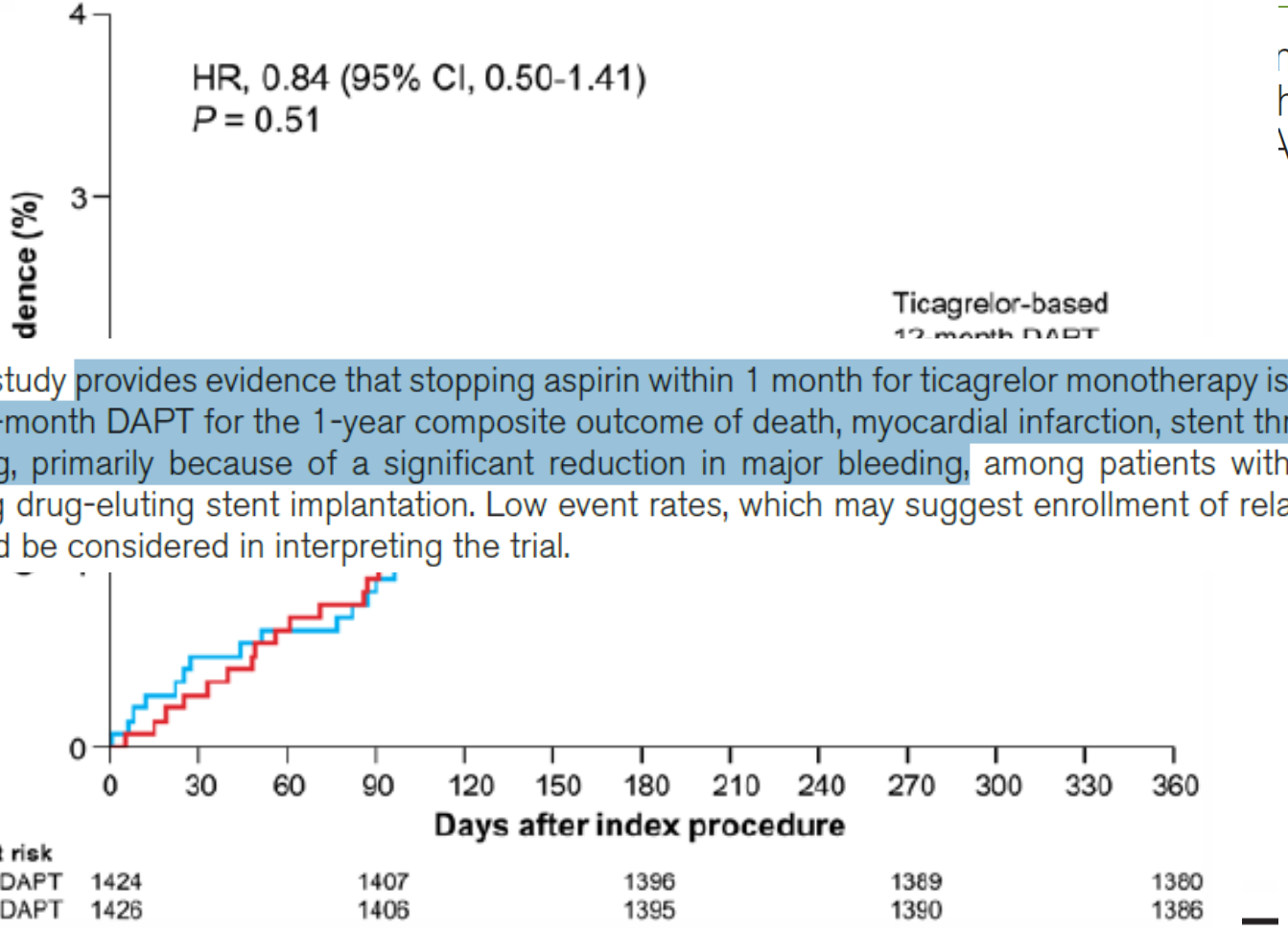

CONCLUSIONS: This study provides evidence that stopping aspirin within 1 month for ticagrelor monotherapy is both noninferior and superior to 12-month DAPT for the 1-year composite outcome of death, myocardial infarction, stent thrombosis, stroke, and major bleeding, primarily because of a significant reduction in major bleeding, among patients with acute coronary syndrome receiving drug-eluting stent implantation. Low event rates, which may suggest enrollment of relatively non–high-risk patients, should be considered in interpreting the trial.

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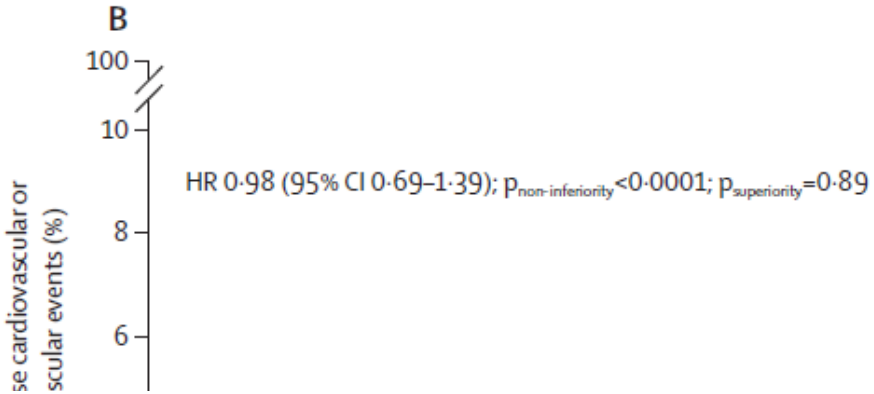

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Interpretation In patients with an acute coronary syndrome who had percutaneous coronary intervention wit contemporary drug-eluting stents and remained event-free for 1 month on dual antiplatelet therapy, treatment wit ticagrelor alone between month 1 and month 12 after the intervention resulted in a lower rate of clinically relevan bleeding and a similar rate of MACCE compared with ticagrelor plus aspirin. Along with the results from previou studies, these findings show that most patients in this population can benefit from superior clinical outcomes wit aspirin discontinuation and maintenance on ticagrelor monotherapy after 1 month of dual antiplatelet therapy.

Time since randomisation (days)

Number at risk (number censored)							
Ticagrelor plus aspirin	1700 (0)	1693 (0)	1684 (1)	1669 (3)	1659 (5)	1648 (7)	1636 (9)
Ticagrelor plus placebo	1700 (0)	1690 (0)	1684 (0)	1673 (1)	1664 (2)	1652 (4)	1640 (6)

Figure 2: Primary efficacy and safety outcomes during follow-up between 1 month and 12 months after percutaneous coronary intervention

DIRETRIZES

1.Sociedade

1. **DAPT p** , com escolha de P2Y

Duração de dupla terapêutica antitrombótica em pacientes com SCASSST em ritmo sinusal – Sumário de recomendações e evidências		
Após SCASSST, é recomendado que a DAPT seja mantida por 12 meses, independentemente da estratégia clínica adotada (angioplastia, cirurgia de revascularização miocárdica ou tratamento clínico).	I	A
Em pacientes com SCASSST e risco aumentado de sangramento, pode-se considerar manter o tempo de dupla antiagregação plaquetária por apenas 6 meses, suspendendo-se o inibidor $P2Y_{12}$ após este período, independentemente da estratégia clínica adotada (angioplastia, cirurgia de revascularização miocárdica ou tratamento clínico)	IIa	B
Em pacientes com SCASSST submetidos à ICP, pode-se considerar manter a DAPT por 3 meses seguido de monoterapia com i$P2Y_{12}$, (preferencialmente ticagrelor).	IIa	A
Associar uma segunda medicação antitrombótica (ver tabela abaixo) ao AAS após os 12 meses de DAP em pacientes com alto risco isquêmico e baixo risco de sangramento.	IIa	A

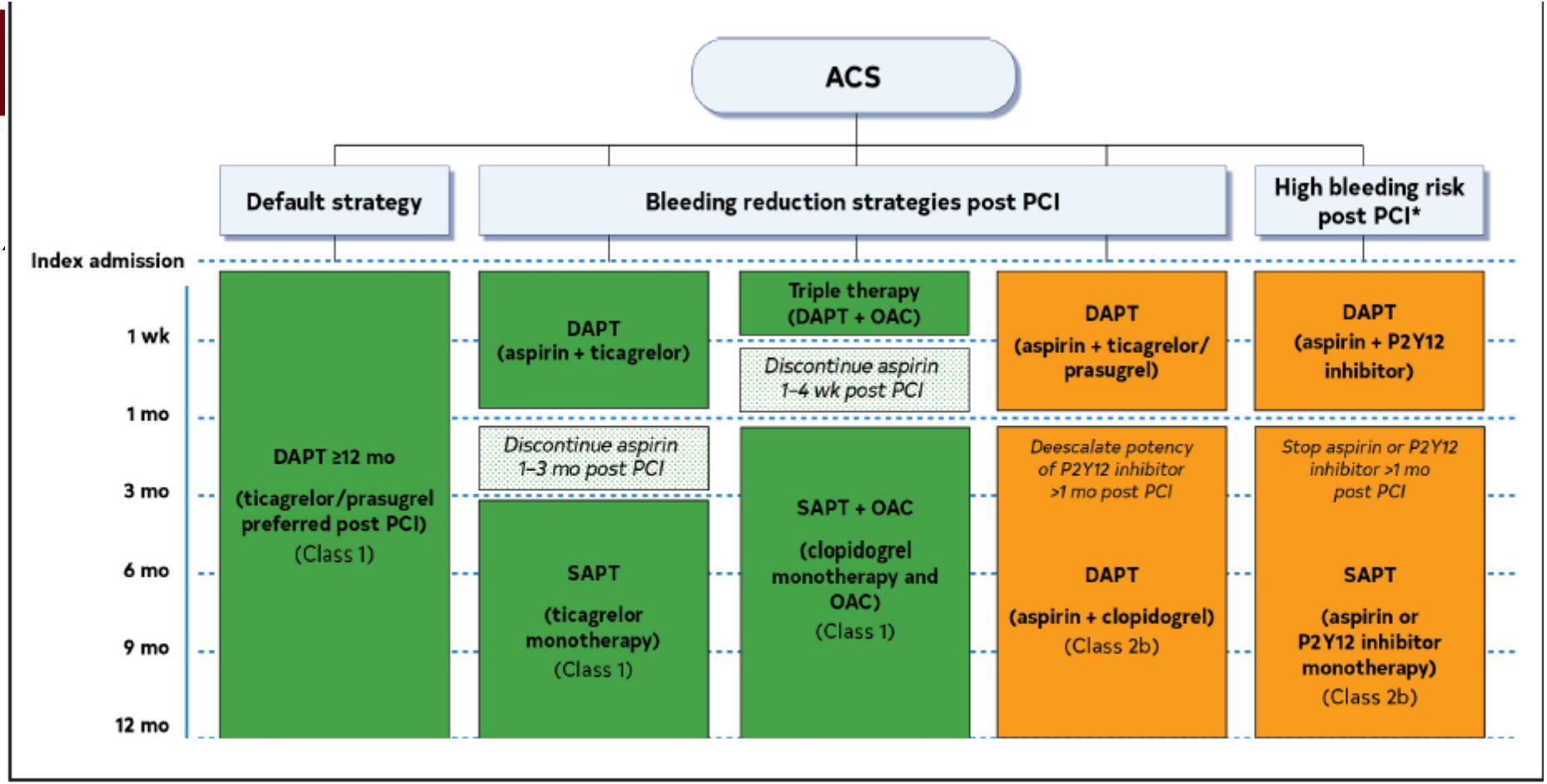

Figure 11. DAPT Strategies in the First 12 Months Postdischarge.

Colors correspond to Class of Recommendation in Table 2. *High bleeding risk discussed in Section 11.1, "Recommendation-Specific Supportive Text" item 5, and outlined in Table 22. ACS indicates acute coronary syndromes; DAPT, dual antiplatelet therapy; OAC, oral anticoagulant; PCI,

OBRIGADO

Antonione Lamartini

antonionelamartini@yahoo.com.br

@lamartini_antonione